REMARKS

By this amendment, claims 2-47 have been cancelled, claims 1 and 48-55 have been amended., and new claims 56-66 have been added. Claims 1 and 48-66 are under consideration.

35 U.S.C. 101 Claim Rejection

Claims 1 and 48-55 stand rejected under 35 U.S.C 101 as directed to non-statutory subject matter. Examiner states that, as filed, claims 1 and 48-55 claim "a cell" which reads on any or all unicellular organisms which are products of nature. Examiner indicates that the recitation of "an isolated or purified cell" to show the hand of man would overcome this rejection.

Applicant has hereby amended 1, 48, and 50- 55 to recite the feature that the cell of the present invention is "an isolated or purified cell". Claim 49, which recites the "insect cell of claim 48" has not been so amended since, by virtue of its dependance on claim 48 (which recites "an isolated or purified cell") the insect cell of claim 49 must also be "an isolated or purified".

In view of the foregoing, Applicant respectfully request withdrawal of this rejection.

35 U.S.C 112, Second Paragraph Rejection

Claims 1 and 48-55 stand rejected under 35 U.S.C.112, second paragraph, for indefiniteness. Examiner states that the claims are indefinite due to the recitation of the phrase "above endogenous levels" in claim 1, and that the meaning of this phrase is unclear. Examiner suggests that if it is the intention is to claim a recombinant or genetically modified cell that produces more CMP-SA than the levels it produced prior to being made recombinant or genetically modified, then the claim should be amended to indicate this feature.

Claim 1 has hereby been amended to recite that the isolated or purified cell of the invention is recombinant or genetically modified, and that the level of CMP-SA produced by the recombinant or genetically modified cell is above that produced before the cell was made recombinant or genetically modified. Further, new claims 57-66 have been added. New claim 57 specifies that the isolated or purified cell is from a recombinant or genetically engineered line of cells which contains and co-expresses the two genes to produce CMP-SA. New claims 58-66 recite various features of such a cell, e.g. as being an insect, yeast, plant, bacterial or fungal cell, identifying the donor substrate as CMP-Neu5 or CMP-KDN , and the two genes as human.

In view of the foregoing, Applicant respectfully request withdrawal of this rejection, and allowance of the new claims.

35 U.S.C 102, Second Paragraph Rejection

Claims 1, 52 and 54 stand rejected under 35 U.S.C 102(b) as anticipated by Munster et al., PNAS, 1998, vol. 95:9140-9145. Examiner states that claim 1 is drawn to a cell producing a donor substrate CMP-SA, CMP-Neu5Ac above endogenous levels, and that Munster et al. disclose two cell types (mutant Chinese hamster ovary cells and mutant/recombinant E. coli cells) both expressing mouse CMP-Neu5Ac leading to accumulation of CMP-SA about endogenous levels. As such, Examiner states that Munster et al. anticipates the subject matter claimed in claims 1, 52 and 54.

Claim 1 has hereby been amended to recite that the cell of claim 1 contains and co-expresses a CMP-sialic acid synthase gene and a sialic acid phosphate synthase gene. In contrast, Munster et al. deal exclusively with cells that are genetically engineered to contain only a CMP-sialic acid synthase gene (murine CMP-Neu5Ac), and neither show nor discuss the desirability of introducing a second gene of any type into the cells. In particular, the sialic acid phosphate synthase enzyme is not discussed by Munster et al. Thus, Munster et al. do not anticipate the subject matter of claim 1 as amended. Furthermore, as discussed in the application at page 96 and shown in Table 5, incorporation of the two genes into the cell allows for a significantly higher level of production of CMP-SA.

Support for this amendment is found in the specification, for example, on page 96 in paragraph 0396 where co-expression of a CMP-sialic acid synthase gene and a sialic acid phosphate synthase gene is discussed. Further, data from cells which co-express the two enzymes is given in the last entry of Table 5, on page 94.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

35 U.S.C 103(a) Rejection

Claims 1, 48-51 and 53 stand rejected under 35 U.S.C 103(a) as unpatentable over Munster et al. (as above) in view of Ogonah et al. (Biotechnol., 1996, vol. 14:197-202) and the common knowledge in the art of molecular biology. Examiner states that the claims 1, 48-51 and 53 teach cells producing a donor substrate CMP-SA, CMP-Neu5Ac, above endogenous levels,

and the cell may be an insect cells (of which four specific examples are listed) of a yeast, plant or fungal cell. Examiner states that Munster et al. teaches such cells when the cells are bacterial or mammalian, but not insect, yeast, plant or fungal cells. However, according to Examiner, Oganah et al. teaches a method to isolate and characterize insect cell lines which are able to perform complex *N*-linked glycosylation of recombinant proteins. Examiner states that the teachings of Munster et al. and those of Ogonah et al. could be combined to result in insect cells with the capacity to sialylate recombinant proteins, and that motivation to develop such an insect cell line. Further, Examiner states that a combination of the teaching of Munster et al. and common knowledge in the art would have obviously resulted in the development of yeast, fungal and plant cells with this same capability.

As discussed above, Munster et al. neither show nor suggest genetically engineering a cell to contain both a CMP-sialic acid synthase gene and a sialic acid phosphate synthase gene. Ogonah et al. describe a study in which the ability of a particular insect cell line, *Estigmena acrea,* to carry out N–glycosylation of a protein (IFN-γ) is studied. The *E. acrea* cell line is not that which is most typically used to for expression of mammalian genes, yet it has been shown to exhibit the capability to carry out complex N–glycosylation reactions. The *E. acrea* cell line used in the study was not genetically engineered to contain additional glycosylation enzymes. Rather, the ability of endogenous enzymes to modify IFN-γ was studied. Ogonah et al. does not show or discuss genetically engineering cells to contain and co-express both a CMP-sialic acid synthase gene and a sialic acid phosphate synthase gene.

Examiner has relied on Ogonah et al. as teaching a source of insect cells for modification by the vector taught by Munster et al. Examiner has further relied on "common knowledge" in the art to provide cells of various other origins (fungal, plant, etc.) for modification by the vector taught by Munster et al. Applicant submits that the combination of Munster et al. and Ogonal et al., or of Munster et al. and common knowledge in the art, would produce only cells of various types transformed with a CMP-Neu5Ac gene, since none of the cited references show or suggest that the modification should take the form of introducing both a CMP-sialic acid synthase gene and a sialic acid phosphate synthase gene. Thus, no combination of these references can render obvious the subject matter of claim 1, which is a cell genetically engineered to contain and co-

express both enzymes.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

Other Matters.

Applicants have hereby amended claim 49 to recite "insect cell" rather than "cell" at the second recitation of the word "cell" in order to maintain consistency of terminology within the claim.

Further, Applicants have hereby amended claim 1 to eliminate the phrase "of interest" as this phrase does not serve to better define any particular feature of the cell of the invention.

Applicant respectfully submits that these two amendments do not constitute the addition of new matter, the one simply adds the word "insect" which already appears in the claim, and the other simply removing a non-descriptive phrase.

Applicant respectfully request entry of these amendments.

New Claim 56.]

New claim 56 recites the case that the genes contained in and expressed by the cell of claim 1 are human genes. Support for this is found in the specification on page 80, first sentence of paragraph 0357 (for SAS) and on page 89, first sentence of paragraph 0379 (for CMP-SAS). Applicant respectfully submits that addition of new claim 56 thus does not constitute the addition of new matter

Formal Matters and Conclusion

In view of the foregoing, Applicant submits that all rejections have been successfully traversed and that claims 1 and 48-55 should be deemed new and unobvious over the prior art of record. The Examiner is respectfully requested to reconsider and pass the above application to issue at the earliest possible time.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at the local telephone number listed below to discuss any other changes deemed necessary in a telephonic or personal interview.

Please charge any underpayment or credit any overpayment of fees to attorney's deposit account #50-2041.

Respectfully submitted,

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APPENDIX A

1. An isolated or purified cell which is recombinant or genetically modified to contain and co-express a CMP-sialic acid synthase gene and a sialic acid phosphate synthase gene, said cell producing the donor substrate CMP-SA above a level produced before said cell was made recombinant or genetically modified.

48. The isolated or purified cell of claim 1, which is an insect cell.

49. The insect cell of claim 48, wherein said insect cell is of a species selected from the group consisting of:

(a) *Spodoptera frugiperda*;

(b) *Tricoplusia ni*;

(c) *Estigmena acrea*; and,

(d) *Drosophila*.

50. The isolated or purified cell of claim 1, which is a yeast cell.

51. The isolated or purified cell of claim 1, which is a plant cell.

52. The isolated or purified cell of claim 1, which is a bacterial cell.

53.The isolated or purified cell of claim 1, which is a fungal cell.

54. The isolated or purified cell of claim 1, wherein the donor substrate CMP-SA is CMP-Neu5Ac (cytidine monophosphate-*N*-acetylneuraminic acid).

55. The isolated or purified cell of claim 1, wherein the donor substrate CMP-SA is CMP-KDN (cytidine monophosphate-2-keto-3-deoxy-D-*glycero*-D-*galacto*-nonoic *acid*).